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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/770,528	01/25/2001	Joseph A. Hedrick	DX0725K2B	7799

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EXAMINER	
KEMMERER, ELIZABETH	

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 11/01/2002

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application N .	Applicant(s)	
	09/770,528	HEDRICK ET AL.	
	Examiner	Art Unit	
	Elizabeth C. Kemmerer, Ph.D.	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 September 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *7-9 and 20-25* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *7-9, 20-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Status of Application, Amendments, And/Or Claims

The amendment filed 17 September 2002 (Paper No. 14) has been entered in full. Claims 1-6 and 10-19 are canceled. Claims 7-9 and 20-25 are under examination.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Withdrawn Objections And/Or Rejections

The objections to the specification for embedded hyperlinks and informalities as set forth at p. 2 of the previous Office Action (Paper No. 11, 05 June 2002) is *withdrawn* in view of Applicant's arguments and amendments (Paper No. 14, 17 September 2002).

The objection to claim 25 for informalities as set forth at p. 2 of the previous Office Action (Paper No. 11, 05 June 2002) is *withdrawn* in view of the amended claim (Paper No. 14, 17 September 2002).

All rejections pertaining to claim 10 as set forth in the previous Office Action (Paper No. 11, 05 June 2002) are *withdrawn* in view of the canceled claim (Paper No. 14, 17 September 2002).

35 U.S.C. § 101 and 112, First Paragraph

Claims 7-9 and 20-25 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a credible, specific and substantial asserted utility or a well established utility.

Claims 7-9 and 20-25 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a credible, specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

The bases for these rejections are set forth at pp. 3-8 of the previous Office Action (Paper No. 11, 05 June 2002).

Applicant's arguments (pp. 3-9, Paper No. 14, 17 September 2002) have been fully considered but are not found to be persuasive for the following reasons.

Quoting from the MPEP and case law, Applicant argues that a disclosed utility corresponding to the claimed subject matter satisfies the utility requirement absent evidence which would cast doubt on the objective truth of the disclosed utility. Applicant urges that the disclosed utility must only be more likely than not true. The examiner takes no issue with Applicant's review of the utility requirement. The specification discloses that the claimed IL-1δ is a new member of the IL-1 family of polypeptides, and that it is involved in inflammation, infectious response and other immunological disorders. In the previous Office Action (pp. 4-5, Paper No. 11, 05 June 2002), evidence was discussed that showed that structural similarity among small soluble proteins such as cytokines is not predictive of functional similarity (see, e.g., Murdoch et al., Ji et al., Tischer et al., Benjamin et al., Vukicevic et al., Massague, Pilbeam et al., and Kopchick et al.). Further, the specification itself admits that the IL-1 family members have distinct activities and bind different receptors (p. 3, lines 15-21, bottom of p. 31, p. 41). Thus, the rejection was proper in rejecting the clams for lack of utility in

the face of evidence which would cast doubt on the objective truth of the disclosed utility. The specification has no further disclosure or working examples regarding the specific biological activities of the IL-1δ polypeptides recited in the claims. If the recited IL-1δ polypeptides have no utility, then the claimed antibodies specific for IL-1δ also have no patentable utility.

Applicant discusses post-filing date references, specifically Debets et al. and Kumar et al., and asserts that these provide supporting evidence of utility for the claimed invention. Applicant argues that Kumar et al.'s IL-1H1 has a sequence which is essentially the same as that of IL-1δ. Applicant states that Kumar et al. confirms that IL-1H1 (or IL-1δ) plays a role in inflammatory responses and viral infection. this has been fully considered but is not found to be persuasive. Kumar et al.'s IL-1H1 does not have a sequence that is essentially the same as instantly disclosed IL-1δ. Kumar et al.'s IL-1H1 is essentially the same as instantly disclosed IL-1ε; however, IL-1ε is not recited in the rejected claims. Specifically, IL-1δ of the instant disclosure is 154 amino acids in length; the IL-1H1 of Kumar et al. is 168 amino acids in length. There are 43 amino acid matches in the alignment of the two sequences (which is essentially identical to the alignment of IL-1δ and IL-1ε in the instant application's Figure 2. Thus, the percent sequence identity between the IL-1δ recited in the claims and Kumar et al.'s IL-1H1 is 43/168 = 26%. In view of the very low degree of sequence similarity between the IL-1δ recited in the instant claims and Kumar et al.'s IL-1H1, as well as the evidence in the art that the IL-1 family members have diverse functions and bind different receptors, the

disclosure of Kumar et al. is not deemed to support the disclosed utility for the IL-1δ recited in the instant claims.

Applicant argues that Debets et al. provides evidence that IL-1δ expression is upregulated in psoriasis (a type of inflammation) and highly expressed in tissues containing epithelial cells (such as lung). Applicant argues that this is consistent with the instant disclosure, pointing to p. 95. This has been fully considered but is not found to be persuasive. Debets et al. is co-authored by several of the instant inventors and clearly discloses further experiments on the instantly disclosed IL-1δ and IL-1ε. It is true that Debets et al. discloses that IL-1δ is expressed at higher levels in psoriasis-diseased tissue than normal skin tissue (see Figure 6). Although this type of correlation between a specific disease state and an alteration in levels of a polypeptide or polynucleotide is generally accepted as a patentable utility, unfortunately this utility is not suggested by the instant application as originally filed. The instant application merely states that IL-1δ is involved in inflammation. It never suggests psoriasis as a specific type of inflammation, and it never states that IL-1δ is expressed at increased levels in psoriasis. Therefore, the specification's assertion that IL-1δ is involved in inflammation is not a substantial utility, because clearly significant further research was required to identify psoriasis as the type of inflammation in which IL-1δ is involved, and that IL-1δ expression levels increased in the psoriasis-diseased tissue. Regarding the increase expression in lung tissue, this is not found to be a specific utility, since many unrelated polypeptides and polynucleotides are expressed differentially. It is also not a

substantial utility, because the significance of the differential expression is not disclosed.

Beginning at p. 6 of the response, Applicant argues that the claimed invention has substantial, specific and credible utilities, namely, chromosomal mapping, tissue distribution, IL-1 receptor binding activity, IL-1 receptor antagonist activity, participation in inflammation or other immunological disorders, and in identifying novel IL-1 receptors. This has been fully considered but is not found to be persuasive for the following reasons. Chromosomal mapping is not a utility applicable to the *claimed* invention, which pertains to antibodies and protein binding compounds, since only nucleic acid probes are used in chromosomal mapping. Tissue distribution is not found to be a specific utility, since many unrelated polypeptides and polynucleotides are expressed differentially. It is also not a substantial utility, because the significance of the differential expression is not disclosed. Regarding IL-1 receptor biding activity, the specification does not disclose exactly which receptor is bound. As discussed at p. 41 of the specification, IL-1 family members bind a diverse group of receptors. Although the specification discusses theories as to how the recited IL-1δ polypeptides bind IL-1 receptor (e.g., Figure 1A), no data is disclosed regarding which IL-1 receptor is bound. Therefore, the assertion that IL-1δ binds and antagonizes IL-1 receptor is not substantial, since significant further research would have been necessary to identify the specific receptor and also binding compounds that have antagonist activity. Regarding the specification's assertion that IL-1δ is involved in inflammation and immunological disorders, it is noted that the specification does not disclose a correlation between any

specific disease state and an alteration in IL-1δ levels or forms. Inflammation and immunological disorders defines an incredibly diverse and large number of specific diseases, including allergy, asthma, infection, injury, and autoimmune diseases. Therefore, this asserted utility is not substantial, since significant further research would have been required to identify a correlation between any specific disease state and an alteration in IL-1δ levels or forms. Regarding the asserted utility that IL-1δ has utility in identifying new IL-1 receptors, this asserted utility is not specific, since any new ligand can be used to identify receptors. It is also not substantial, because significant further research would have been required to determine the significance of IL-1δ and any new receptors to which it bound.

Beginning at p. 7 of the response, Applicant discusses he references cited in the previous Office Action. Applicant characterizes Murdoch et al., Ji et al., Tischer et al., Vukicevic et al., and Massague as only suggesting that structurally related members of some specific cytokine families may not share conserved functional properties. Applicant urges that they do not indicate that conserved functional properties are not present in members of other cytokine families such as IL-1. This is not found to be persuasive. Murdoch et al., Ji et al., Tischer et al., Benjamin et al., Vukicevic et al., Massague, Pilbeam et al., and Kopchick et al. demonstrate that structural similarity is not predictive of functional similarity in a wide variety of soluble growth factor-like proteins such as cytokines. Additionally, the literature indicates that the IL-1 family has members with diverse functions, as acknowledged by the specification (p. 3, lines 15-21 and bottom of p. 31). The literature also reports that different IL-1 family members bind

different receptors, also as acknowledged by the specification (p. 41). Therefore, the evidence as a whole indicates that the logic underlying the asserted utilities of the present invention (i.e., that IL-1δ has IL-1 activities based on its structural similarity to other IL-1 family members) is seriously flawed.

Applicant argues that Skolnick et al., Bork et al. and Brenner et al. relate only to general technical fields or molecule biology and biochemistry, and are not specific to the instant subject matter. This is not found to be persuasive. Skolnick et al., Bork, Doerks et al., Smith et al., Brenner and Bork et al. all report that caution should b taken when asserting that a new protein has functional similarity to proteins in the sequence databases for several important reasons (see previous Office Action, pp. 5-6). Since the instant application asserts that IL-1δ has IL-1 activities based on its structural similarity to other IL-1 family members found in the sequence databases, the teachings of these references are directly on point.

Beginning at p. 8 of the response, Applicant provides arguments concerning the scope of claim 7. It appears that the Applicant may have misinterpreted the issue regarding claim 7 raised in the previous Office action. Claim 7 reads: "A binding compound comprising an antigen binding site from an antibody, which specifically binds to **a mature polypeptide *comprising* at least 8 contiguous amino acid residues from SEQ ID NO: 2**" (emphasis added). The portion of the claim written in bold type can be broadly but reasonably interpreted as reading on chimeric polypeptides comprising at least 8 amino acid residues of SEQ ID NO: 2. However, the claim only requires that the binding compound bind the polypeptide as a whole. Therefore, the

claim reads on binding compounds that specifically bind sequences from the polypeptide that *flank* the "at least 8 contiguous amino acid residues of SEQ ID NO: 2." Amending the claim to include a phrase such as "wherein said antigen binding site specifically binds an epitope located within said 8 contiguous amino acid residues" is one way of resolving this issue specific to claim 7. Of course, if the suggested amendment is adopted, claim 7 would still be rejected under 35 U.S.C. §§ 101 and 112, first paragraph, for lack of utility and enablement, due to the other issues discussed above. If Applicant has any questions regarding this specific issue for claim 7, Applicant is invited to telephone the examiner for an interview.

Conclusion

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Elizabeth C. Kemmerer, Ph.D. whose telephone number is (703) 308-2673. The examiner can normally be reached on Mon. - Thurs., 6:30 to 4:00, and alternate Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne L. Eyler, Ph.D. can be reached on (703) 308-6564. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Elyabeth C. Kemmerer

ECK
November 1, 2002